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EXAMINER

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Please find below and/or attached an Office communication concerning this application or proceeding.

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/582,342
Filing Date: September 18, 2000
Appellant(s): BRANDS, RUDI

Jennifer R. Leach
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 3/6/2009 appealing from the Office action mailed 5/7/2009.

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(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

A substantially correct copy of appealed claims 39-44 appears on page 18 of the submission of 5/7/2009. The minor errors are as follows: the status identifier of claims 39-44 is inaccurate; claims 39-44 have been **Previously Presented**.

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(8) Evidence Relied Upon

Griffiths et al. "Scale-up of Suspension and Anchorage-Dependent Animal Cells in Basic Cell Culture Protocols." Basic Cell Culture Protocols. Ed. J.W. Pollard and J.M. Walker. Totowa, NJ: Humana Press, 1997. pp. 59-75.

(No Author) "Amish Friendship Bread" Wikipedia.org. 17 July 2007. Wikimedia Foundation, Inc. Accessed 6 August 2007 from URL: <http://en.wikipedia.org/wiki/Amish_Friendship_Bread>.

(No Author) "Friendship Cake/Bread History" Recipe Circus.com. (No publishing date). The Recipe Circus. Accessed 6 August 2007 from URL: <http://recipecircus.com/recipes/philocrates/Hint/Friendship_CakeBread_History.html>.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 39-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (Scale-up of Suspension and Anchorage-Dependent Animal Cells in Basic Cell Culture Protocols, Edited by Pollard et al. Humana Press Inc., 1997, pp.59-75), in light of the discussion of the history of sourdough or "Amish Friendship Bread" recited in "Friendship Cake/Bread History" (from <http://recipecircus.com>) and "Amish Friendship Bread" (from <http://en.wikipedia.org>).

Griffith et al disclose methods for preparing cultures of anchorage-dependent cells for the production of biological products, comprising inoculating cells onto a substrate, such as a roller bottle (solid support) or microcarrier beads (particulate matter), culturing the cells until they reach confluence, removing the culture media, adding trypsin to the cell culture to release the cells from the substrate, then

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passaging the cells (wherein 'passaging' involves splitting the culture and re-seeding and culturing at least one portion of the split culture) (See Griffiths et al, Section 3.2 "Anchorage-Dependent Culture" Pgs 65-71; especially Section 3.2.1.1.1 "[Roller Culture] Procedure" (at Pg. 67), Section 3.2.1.2.1 "[Glass Bead Immobilized Beds] Procedure" (at Pgs. 67-71) and Section 3.2.1.3.2 "[Microcarrier Culture] Procedure" (at Pg. 70-71)). The initial cell culture of Griffith et al reads on what Applicants are calling the 'preproduction batch', the passaged cells (i.e. cells re-seeded after splitting) read on what Applicants are calling the 'production batch'.

Griffith et al differ from the instant invention only in that, while they disclose passaging the cells of their 'preproduction batch', they do not explicitly state a first portion of the cells are replated as a seed for a subsequent 'preproduction batch', and a second portion of the recovered cells are transferred and used as a 'production batch' specifically for the production of biological products, which Applicants are calling a 'repeated discontinuous process'.

However, it is maintained that replating a portion of the cells as a seed for subsequent 'preproduction batches', and transferring a second (larger) portion of cells for use as a 'production batch' for production of biological products produced by the cells (*i.e.* performing a repeated discontinuous process), would have been routinely performed by one of ordinary skill in the art, and therefore the invention is held to be *prima facie* obvious. The concept of splitting a culture, using the majority of it for production of a biological product, and retaining and maintaining smaller portion as a seed culture is a routine method in the art. Due to the fact that such is so well known, it is not routinely included in written protocols intended for artisans of ordinary skill. To exemplify its commonplace in the art, processes for production of sourdough or "Friendship Bread" (See, for example, "Friendship Cake/Bread History" from <http://recipecircus.com> (accessed 8/6/2007), or the discussion at Wikipedia under "Amish Friendship Bread" (accessed 8/6/2007)) is referenced: Production of sourdough bread involves dividing of a starter culture (a 'preproduction batch') into two portions, using one portion for the production of the

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bread, and sharing the other portion with a friend, wherein the friend can repeat the process; in such a manner single cultures can exist for years. In this case the portion retained by the originator is considered the 'production batch', as it is used to produce bread; the portion given away is considered to be a seed for the production of at least one subsequent 'preproduction batch', as the friend is to repeat the process.

In the method of Griffiths et al, one of ordinary skill in the art would have been motivated to retain and reseed at least one portion of the culture as a seed for future 'preproduction batches' in order to continue the cell line, thereby saving money (by not needing to purchase a subsequent cell culture seed), and increasing the amount of biological product which can ultimately be produced (as the initial culture is not exhausted after the first round of biological product production, but a small portion can be retained, passaged and expanded, so as to provide a cell source for future 'production batches'). One would have had a reasonable expectation of successfully carrying out this 'repeated discontinuous process' because the steps of splitting and passaging cell cultures, as well as steps for obtaining biological products from a 'production culture' were well known in the art (see, e.g. Griffith et al), and are even regularly carried out by non-skilled artisans (such as in the process of passing on sourdough starter cultures).

Therefore, the instantly claimed method is not considered to be patentable, as it was obvious to one of ordinary skill at the time the invention was made. One would have known how to culture anchorage-dependent cells to produce a biological product, as illustrated by Griffith et al and it would be well within the purview of the skilled artisan, and generally common sense, to maintain a portion of the cell culture during each split, to replenish the original culture and use to repeat the process, thereby prolonging the culture life and increasing the amount of culture which can be used to produce the desired product.

It is further pointed out that this rationale relies on common sense and the knowledge generally available to the skilled artisan must be taken into account; such may be taken into consideration as rationale for rendering an invention patentable per the Supreme Court decision of *KSR International Co*

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vs. Teleflex Inc. Specifically, the Supreme Court held that “Variations of particular work available in one field of endeavor may be prompted by design incentives and other market forces, either in same field or different one, and if person of ordinary skill in art can implement predictable variation, 35 U.S.C. §103 likely bars its patentability; similarly, if particular technique has been used to improve one device, and person of ordinary skill would recognize that it would improve similar devices in same way, then using that technique is obvious unless its actual application is beyond person's skill, and court resolving obviousness issue therefore must ask whether improvement is more than predictable use of prior art elements according to their established functions.” See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) at 1386.

Finally, with regards to the production of viruses as the specific biological product, it is noted that the methods of Griffith et al and Pollard et al are applicable to all anchorage-dependent cell types. Furthermore, anchorage-dependent cells that are routinely cultured to product viruses are also known in the art. For example, MDCK cells are notoriously old and well known in the art for their use in culture to grow viruses (dating back to at least the 70s). Therefore it would have been obvious at the time the invention was made to split and passage MDCK cells, per the repeated discontinuous culture process discussed above for the production of viruses.

Accordingly, the claimed invention is found to be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

(10) Response to Argument

Appellants argue the Examiner has failed to establish a *prima facie* case of obviousness over the cited references.

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Appellants first assert that the cited references fail to teach or suggest all claim limitations. Specifically, Appellants assert that Griffiths fails to disclose splitting the cells into two parts in the manner claimed, but rather only addresses the cells as a single "part". Appellants also assert the process of Griffiths et al is not a 'discontinuous procedure'.

In response to Griffiths et al not disclosing 'splitting' the cells, it is submitted that Griffiths et al recite the cells, once detached via enzymatic action, are "harvested, diluted in fresh medium and serum, and passaged on" (See Griffiths et al, Pg. 67, step #6). Passaging of cells is a term of art which involves (as stated by Griffiths et al) dilution in fresh media and subsequent seeding of a portion of the diluted cell culture. Splitting of the cell culture is an inherent aspect of passaging, as it is required to reduce the cell concentration in order to maintain cell viability.

Appellant's assertion that the handwritten note on Page 67 of Griffith et al referencing a 'discontinuous procedure' is inaccurate, such is not being addressed because the rejection of record fully addresses the claims. The subject matter of the handwritten note (by a previous examiner) is considered immaterial.

In response to Griffiths et al not disclosing a repeated discontinuous process, such is acknowledged. Griffiths et al are not cited as anticipating the claimed rejection, but rather the claimed invention is considered to be *prima facie* obvious over the basic protocol taught by Griffiths et al, and the knowledge generally available to those skilled in the art (with regards to repeatedly passaging cultures to maintain the cell culture, and to harvesting biological products from cell cultures for commercial interests.)

Appellants secondly assert the Examiner has failed to meet her burden under the TSM rationale. However, Appellants' arguments appear to be based on the cell cultures of primary reference Griffiths et al being non-analogous to the bread preparation discussed in the secondary references, and thus one in the

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field of cell culture would not look to the field of bread preparation, nor would one have a reasonable expectation of successfully employing the techniques utilized in the bread preparation in a scale-up procedure for cell culture for production of a biological.

In response, it is submitted that sourdough starter is actually a cell culture, it is an active yeast culture, and therefore is relevant to the art of cell culture in at least as far as it pertains to methods of propagating a cell culture. Furthermore, it is submitted that the discussion of sourdough friendship bread was only relied upon to show the extreme commonness of the idea of 'repeated discontinuous' processes of culture. Still further, it has been held that "[W]hen a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability." See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) at 1396. Thus, even if one were to interpret propagation of sourdough starter culture as being non-analogous to cell culture, modifications and variations to improve methods can be imported across different fields of art.

Appellants thirdly assert the art teaches away from the claimed invention. Specifically, Appellants assert that difficulties were recognized with scaling-up anchorage-dependent cell cultures for production of biologicals. Appellants cite Griffiths et al and Groner et al in support. Appellants assert that the recognized difficulties in scaling-up of anchorage-dependent cell culture is a teaching away from the claimed invention

In response, it is noted that the prior art, including Griffiths et al, recognized technical difficulties with scaling-up of anchorage-dependent cell culture; however Griffiths et al is specifically directed to methods to overcome these technical difficulties, thus the prior art does not teach away, but specifically teaches known methods of addressing the technical difficulties.

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Finally, Appellants argue they have rebutted any *prima facie* case of obviousness based on a showing of satisfying a long-felt need, as the claimed method permits production of large quantities of biologicals from cell cultures in a short period of time.

In response, it is submitted that Appellants have not established a long-felt need. Establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution. Appellants have not established evidence of such. Biological products from cells are routinely made in large quantities, as methods of scale-up procedures for both suspension- and anchorage-dependent cell cultures were known (See, e.g. Griffiths et al). Furthermore, the instant case is considered to be a situation where the concept of the invention was, in fact, so well known, that specific disclosure of such in written protocols was generally unnecessary. Skilled artisans recognize that to continuously produce a desired biological product in culture, the culture must be continually tended to, maintained and replenished when exhausted, due to the need to replenish, a stock started culture would routinely be maintained. Therefore the *prima facie* case of obviousness has not been successfully rebutted.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

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For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Allison M. Ford/

Primary Examiner, Art Unit 1651

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